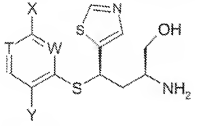
Amendments to the Claims:

This listing of claims replaces all prior versions and listings of claims in the application:

Listing of Claims:

1. (Currently Amended) A compound of formula (I)



(I)

wherein:

T and W independently represent CR^1 ~~or N~~; and when more than one R^1 group is present, each may be selected independently;

X and R^1 independently represent H, C1 to 4 alkyl, C1 to 4 alkoxy, halogen, CN, C≡CH, NO_2, CHO, $COCH_3$ or NHCHO; said alkyl or alkoxy group being optionally further substituted by one or more fluorine atoms;

Y represents C1 to 4 alkyl, C1 to 4 alkoxy, halogen, CN, C≡CH, NO_2, CHO, $COCH_3$ or NHCHO; said alkyl or alkoxy group being optionally further substituted by one or more fluorine atoms;

or a pharmaceutically acceptable salt thereof.

2. (Original) A compound according to Claim 1 wherein Y represents CN or halogen.

3. (Previously Presented) A compound according to Claim 1 wherein X and R^1 independently represent H, halogen or CF_3.

4. (Original) A compound of formula (I), according to Claim 1, which is:

2-[[(1*R*,3*S*)-3-amino-4-hydroxy-1-(5-thiazolyl)butyl]thio]-5-chloro-3-pyridinecarbonitrile;

2-[[(1*R*,3*S*)-3-amino-4-hydroxy-1-(5-thiazolyl)butyl]thio]-4-chloro-benzonitrile;

(2*S*,4*R*)-2-amino-4-[[2-chloro-5-(trifluoromethyl)phenyl]thio]-5-thiazolebutanol;

2-[[(1*R*,3*S*)-3-amino-4-hydroxy-1-(5-thiazolyl)butyl]thio]-6-(trifluoromethyl)- 3-pyridinecarbonitrile;

2-[[(1*R*,3*S*)-3-amino-4-hydroxy-1-(5-thiazolyl)butyl]thio]-5-chloro-benzonitrile;

or a pharmaceutically acceptable salt thereof.

5. (Cancelled)

6. (Previously Presented) A pharmaceutical composition comprising a compound of formula (I) according to Claim 1, or a pharmaceutically acceptable salt thereof, in admixture with a pharmaceutically acceptable adjuvant, diluent or carrier.

7-12. (Cancelled)

13. (Withdrawn) A method for the treatment or prophylaxis of pain comprising administering a compound of formula (I) as defined in Claim 1, or a pharmaceutically acceptable salt thereof.

14. (Withdrawn) A method for the treatment or prophylaxis of an inflammatory disease comprising administering a compound of formula (I) as defined in Claim 1, or a pharmaceutically acceptable salt thereof, and a COX-2 inhibitor.

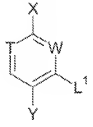
15. (Withdrawn) A method of treating, or reducing the risk of, a human disease or condition in which inhibition of nitric oxide synthase activity is beneficial which comprises administering a therapeutically effective amount of a compound of formula (I), as defined in Claim 1, or a pharmaceutically acceptable salt thereof.

16. (Withdrawn) A method according to Claim 15 in which it is predominantly inducible nitric oxide synthase that is inhibited.

17. (Previously Presented) A method of treating an inflammatory disease selected from the group consisting of inflammatory bowel disease, rheumatoid arthritis, and osteoarthritis in a person suffering from-said disease, wherein the method comprises administering a therapeutically effective amount of a compound of formula (I), as defined in Claim 1, or a pharmaceutically acceptable salt thereof.

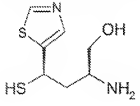
18. (Previously Presented) A process for the preparation of a compound of formula (I), as defined in Claim 1, or a pharmaceutically acceptable salt, enantiomer or racemate thereof, wherein the process comprises:

(a) reaction of a compound of formula (II)



(II)

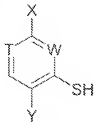
wherein T, X, Y and W are as defined in Claim 1 and L^1 represents a leaving group, with a compound of formula (III)



(III)

or

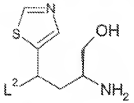
(b) reaction of a compound of formula (IV)



(IV)

wherein T, W, X and Y are as defined in Claim 1,

with a compound of formula (V)



(V)

wherein L^2 is a leaving group.

19. (Withdrawn) A process as defined in Claim 18, further comprising:

converting the resultant compound of formula (I) into a pharmaceutically acceptable salt thereof; converting the resultant compound of formula (I) into another compound of formula (I); or converting the resultant compound of formula (I) into an optical isomer thereof.

20. (Previously Presented) A compound according to Claim 2, wherein X and R^1 independently represent H, halogen or CF_3.

21. (Previously Presented) The method as claimed in Claim 17, wherein the inflammatory disease is inflammatory bowel disease.

22. (Previously Presented) The method as claimed in Claim 17, wherein the inflammatory disease is rheumatoid arthritis.

23. (Previously Presented) The method as claimed in Claim 17, wherein the inflammatory disease is osteoarthritis.

REMARKS

Applicant has amended claim 1 to remove non-elected subject matter. No new matter has been introduced by this amendment.

Claims 1-4, 6, 17, 18, and 20-23 are now pending. Reconsideration of the application, as amended, is requested in view of the remarks below.

Rejection under 35 U.S.C. 112, first paragraph

Claims 17 and 21-23 are rejected for lack of adequate enablement. Specifically, the Examiner points out that "[t]he claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention."

I

To support her rejection, the Examiner relies on the eight factors set forth in *In re Wands* 8 USPQ2d 1400 (CAFC, 1988). Applicant traverses below.

(1) Nature of the invention

The invention relates to treatment of inflammatory disease (in particular, inflammatory bowel disease, rheumatoid arthritis, and osteoarthritis) using the compounds of formula (I) shown in claim 1, which are nitric oxide synthase (NOS) inhibitors.

(2) and (3) State of the prior art and predictability and lack thereof in the art

According to the Examiner, the degree of the unpredictability in the relevant art is high.

Applicant would like to point out that it is well established in the art that NO and NOS are linked to the pathogenesis of inflammatory diseases. For example, IDrug 2001, 4(7): 793-803 by Cheshire (which has been cited by the Examiner) teaches that *in vivo* experimental results showed that NOS inhibitors can be used to treat a variety of inflammatory disease, including inflammatory bowel disease, rheumatoid arthritis, and osteoarthritis recited in claim 17. See the Introduction section and the references cited therein. As another example, WO 00/13709 (a copy of which is attached hereto as "Exhibit A") demonstrates that an NOS inhibitor, N-iminoethyl-L-lysine, showed *in vivo* efficacy in treating osteoarthritis and suggests that NOS inhibitors in general can be used to treat this disease. See, e.g., page 4, lines 5-13 and page 6, lines 7-23.

This invention is based on the discovery that certain compounds covered by formula (I) inhibit NOS activity. In view of the prior art mentioned above, a skilled person would be able to extrapolate the compounds' inhibitory effect on NOS to their anti-inflammatory activity.

(4) and (5) Amount of direction or guidance and working examples

The specification provides synthetic examples of making compounds called for in claims 17 and 21-23 and *in vitro* examples of testing these compounds for their inhibitory activity against NOS. In addition to those examples, the specification also provides general guidance of how to make the compounds and how to use them for the asserted utilities (page 6, line 8 through page 9, line 1 and page 12, lines 9-27). All the techniques mentioned in the examples and general guidance are routine. Following the guidance and working examples, a skilled person in the art, without undue experimentation, would be able to understand how to make and how to use this invention. In other words, there are sufficient guidance and working examples in the specification to enable a skilled person to practice this invention.

The Examiner asserts that "[t]he specification is silent as to whether [] any compound treats [] inflammatory bowel disease, rheumatoid arthritis or osteoarthritis." It appears to be her position that, to support the claims, Applicant needs to provide *in vivo* examples showing efficacy of the compounds in treating inflammatory bowel disease, rheumatoid arthritis, and osteoarthritis. Applicant disagrees.

According to MPEP 2107.03,

> "[i]f **reasonably correlated** to the particular therapeutic or pharmacological utility, data generated using ***in vitro*** assays, **or** from testing in an animal model **or** a combination thereof almost invariably will be sufficient to establish therapeutic or pharmacological utility for a compound, composition or process" (emphases added).

As mentioned above, it is well established from the *in vivo* experimental results shown in the prior art that inhibition of NOS activity generally leads to treatment of inflammatory disease, in particular, inflammatory bowel disease, rheumatoid arthritis, and osteoarthritis. Working examples of this application show that compounds of formula (I) are effective in inhibiting NOS activity in an *in vitro* assay. Clearly, a **reasonable correlation** between the *in vitro* efficacy and

the claimed treatment has been established. In sum, the working examples sufficiently support the scope of the claims.

(6) Breadth of the claims

As a result of removal of "reducing the risk of," claim 17 has been limited to treatment of inflammatory disease. Claims 21, 22, and 23 have also been limited to treatment of inflammatory bowel disease, rheumatoid arthritis, and osteoarthritis, respectively. As discussed above, the working examples and general guidance provided in the specification sufficiently support the scope of the claims. Claims 17 and 21-23 are not overly broad.

(7) and (8) Level of skill in the art and quantity of experimentation

The art relevant to this invention includes synthetic chemistry and medical biology. All of the techniques needed to practice this invention are routine procedures and therefore do not require a person of extraordinary skill.

Applicant would like to bring to the Examiner's attention a statement cited in a Federal Circuit decision: "[a] considerable amount of experimentation is permissible, if it is merely routine, or if the specification in question provides a reasonable amount of guidance with respect to the direction in which the experimentation should proceed." *In re Wands*, 8 USPQ2d 1400, 1404 (CAFC 1988), citing *In re Jackson*, 217 USPQ 804, 807 (CCPA 1969).

As discussed above, the specification provides both general guidance and working examples of synthesizing and screening compounds, both of which are routine procedures well known in the art. Given this routine nature, the amount of experimentation required to practice the claimed invention, whether considerable or not, is by no means undue.

II

Having considered the eight Wands factors, Applicant submits that the specification provides adequate enablement for the claimed invention.

Rejection under 35 U.S.C. § 103(a)

Claims 1-4, 6, 17, 18, and 20-23 were rejected under 35 U.S.C. § 103(a) in view of Birkinshaw et al., WO 02/090332 ("Birkinshaw").

The present application claims priority to PCT/SE2003/001712, filed November 6, 2003, which in turns claims priority to Swedish Patent Application Serial No. 0203304.1, filed

November 7, 2002. The subject matter covered by claims 1-4, 6, 17, and 20-23 is described in Swedish Patent Application Serial No. 0203304.1. Therefore, these claims are entitled to an effective filing date of November 7, 2002.

Birkinshaw was filed on May 6, 2002 and published on November 14, 2002. As it was published after, but filed before, the effective filing date of the present application, it is only citable as a 35 U.S.C. § 102(e) reference, but not as a 35 U.S.C. §102(a) or 35 U.S.C. § 102(b) reference.

35 USC §103(c) provides that prior art under 102 (e), (f), and (g) cannot be used as §103 prior art against a claimed invention if the claimed invention was, at the time the invention was made, owned by, or subject to an obligation of assignment to the same person or company.[1] As discussed above, Birkinshaw only qualifies as a 102(e) reference. Further, since the inventors named in Birkinshaw and the inventor named in the present application were under an obligation, by virtue of their employment, to assign their inventions to AstraZeneca AB. Thus, based on 35 USC §103(c), Birkinshaw does not qualify as a 103(a) reference. Accordingly, the 35 U.S.C. § 103(a) rejection should be withdrawn.

Double-patenting rejection

Claims 1-4, 6, 17, 18, and 20-23 have been rejected provisionally for obviousness-type double patenting in view of the claims in co pending U.S.S.N. 10/476,958. Applicant will address this rejection once the present claims are deemed otherwise allowable.

[1] See also MPEP, 706.02(l)(1)(I), which states that effective November 29, 1999, subject matter which was prior art under former 35 U.S.C. § 103 via 35 U.S.C. 102(e) is now disqualified as prior art against the claimed invention if that subject matter and the claimed invention "were, at the time the invention was made, owned by the same person or subject to an obligation of assignment to the same person."